Case Report



# Delayed Traumatic Rupture of the Spleen in a Patient with Mantle Cell Non-Hodgkin Lymphoma after in-hospital fall: a fatal case

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# Delayed Traumatic Rupture of the Spleen in a Patient with Mantle Cell Non-Hodgkin Lymphoma after In-Hospital Fall: A Fatal Case

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**Abstract:** Splenic rupture and hematoma are significant complications that can arise in patients with non-Hodgkin lymphoma (NHL). Understanding these associations is essential for optimal patient management and patients' enhancing outcomes. Histopathological and immunohistochemistry analyses are crucial in diagnosing NHL and assessing splenic involvement. A judicial autopsy was requested by the Prosecutor's Office for a malpractice claim due to a fall in the hospital. In the Emergency Department, a 72-year-old man fell from the gurney, reporting a wound to his forehead. No other symptoms were reported. A face and brain CT scan showed no abnormalities. Nine days after discharge, the patient presented with abdominal pain. Abdominal CT revealed splenic rupture and hemoperitoneum. The patient underwent open splenectomy, but the patient showed signs of hemodynamic shock and subsequently died. The evidence emerging from the autopsy allowed us to diagnose a Mantle Cell non-Hodgkin lymphoma with spleen involvement, previously unknown. Histopathological and immunohistochemical analyses were performed to assess splenic rupture's diagnosis and time estimation. The findings strongly suggest that the splenic rupture was associated with the patient's fall and the pre-existing malignancy. This case highlights the importance of considering underlying hematological malignancies when investigating delayed splenic rupture. Immunohistochemical study of spleen samples allowed the assessment of the timing of splenic hematoma and rupture, leading to establishing a causal relationship with trauma.

**Keywords:** hospital fall; delayed splenic rupture; non-hodgkin lymphoma; autopsy; forensic diagnosis; malpractice; immunohistochemistry

## 1. Introduction

Splenic ruptures typically occur after direct traumatic injury to the abdomen. However, the majority of traumatic splenic ruptures represent an acute event; a minority of patients present with a two-stage splenic rupture that occurs days to weeks later than abdominal trauma. [1]. According to Baudet, the period from trauma to splenic rupture can be 48 hours or more and is characterized by a variable asymptomatic period [2]. 50% of patients experience hemorrhage within one week after the trauma, 25% within two weeks, and 10% of cases in more than four weeks. Patients who develop an

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early rupture of the spleen die at a rate of around 1%, while the mortality associated with delayed rupture is approximately 15% [3–5].

Splenic rupture can also develop in the absence of trauma, although it is an infrequent event. Several pathologies have been associated with splenic rupture in the absence of trauma, most often malignant hematological disorders, viral infections, or local inflammatory disorders [6].

Among malignant hematological disorders involved in splenic rupture, non-Hodgkin lymphoma (NHL) (34%) and acute myeloid leukemia (34%) are most frequently reported, followed by chronic myeloid leukemia (18%) and lymphoblastic acute leukemia. [7] This occurs due to the possible splenic involvement of these disorders, which determine congestion of the splenic parenchyma by blast cells. Therefore, from what emerges from Scientific literature, spleen rupture and hematoma are significant complications that can arise in patients with NHLs [8]. In some cases, NHL can also cause splenomegaly, making it more susceptible to rupture due to trauma or even spontaneously [9,10]. The rupture may lead to intraperitoneal bleeding, forming a hematoma. Histopathological and immunohistochemistry analyses play a crucial role in diagnosing NHL and assessing the extent of spleen involvement [10]. Identifying such complications is essential for timely intervention and optimal patient management. In this regard, previous research underscored the significance of conducting histochemical and immunohistochemical analyses on sub-capsular splenic hematoma. This has yielded valuable findings for determining the timeline of sub-capsular hematoma development despite the necessity to establish the causal link between splenic rupture and a preceding traumatic incident [11]. Understanding these associations can enhance patient care and outcomes and establish causal relationships in a forensic context. This report aims to explore the histopathological and immunohistochemical aspects involved in diagnosing traumatic splenic rupture in a patient with mantle cell non-Hodgkin lymphoma who died ten days after a fall in the hospital in a Judicial autopsy case of medical malpractice.

## 2. Case Report

A 72-year-old male was admitted to the hospital with a history of asthenia and hypotension for several days. While he was at the Emergency Department (ED), he fell from the gurney, reporting a lacerated contused wound to his forehead. No other symptoms were reported, and a CT scan of the face and brain showed no abnormalities. No significant clinical and blood test elements suggest urgency and vital signs were normal. Therefore, he was discharged. Nine days after discharge, the patient presented with abdominal pain, pallor, and dyspnea, and he was taken to the emergency room. Abdominal CT revealed splenomegaly, splenic rupture, and hemoperitoneum. An emergent open splenectomy was performed, but the patient showed signs of shock and hemodynamic instability. After surgery, he was transferred to the intensive care unit, and subsequently, the death occurred as a consequence of hemorrhagic shock.

The prosecutor officer requested a judicial autopsy for a malpractice claim due to the fall in the ED and a lack of surveillance. All the medical records were analyzed. At the time of the autopsy, the spleen, which was removed during the life-saving operation, was examined macroscopically. All organs and tissue samples were routinely fixed in 10% neutral buffered formalin. Microscopic examination was carried out with different histochemical and immunohistochemical stainings.

We performed haematoxylin-eosin staining and histopathological time estimation of the subcapsular hematoma and hemorrhage with van Gieson staining and CD68 expression. Immunohistochemistry targeted multiple lymphoma markers for lymph nodes, spleen, and bone marrow samples, such as CD20, CD5, CD3, CD10, Bcl-2, BCl-6, and Ki-67.

### *2.1. Autopsy Findings*

At the time of the autopsy, the corpse appeared well preserved with no signs of putrefaction. The height was 170 cm, and the corpse weighed 100 kg. The corpse showed signs of laparotomy. Furthermore, on the forehead, there was a sutured lacerated contused wound measuring 2.5 x 0.5 cm.

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The autopsy revealed an increased volume of paratracheal and mesenteric lymph nodes that were taken for histological investigation and blood and blood clots in the splenic lodge (Figure 1). No other significant macroscopic findings were identified.

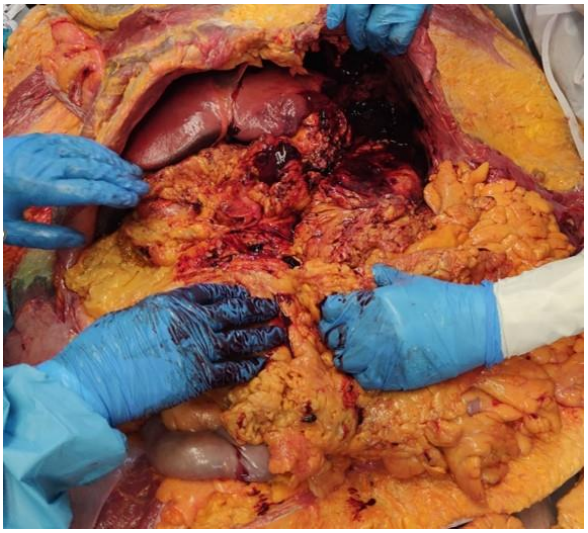

**Figure 1.** Blood clots in the splenic lodge.

After fixation in formaldehyde solution, the spleen measured 24 x 12 x 18 cm (Figure 3) and weighed 413 grams. Macroscopic examination of the spleen showed severe splenomegaly with a subcapsular hematoma (Figures 2 and 3). On the convex surface of the organ, there was a 5 cm capsular laceration (Figure 3). Along the convex surface, there were multiple subcapsular infarcted areas, greyish. On the section surface (through cuts along the minor axis), there were areas of hemorrhagic dissection underlying the superficial laceration that extended almost to the total thickness of the organ (Figure 3). From the convex to the concave margin, there were infarcted areas greyish in color and map-like appearance (Figure 3), ranging in size from 2 cm to 8 cm. There were multiple areas of hemorrhagic infarction in the subcapsular area, affecting the hilar surface and the upper pole of the organ.

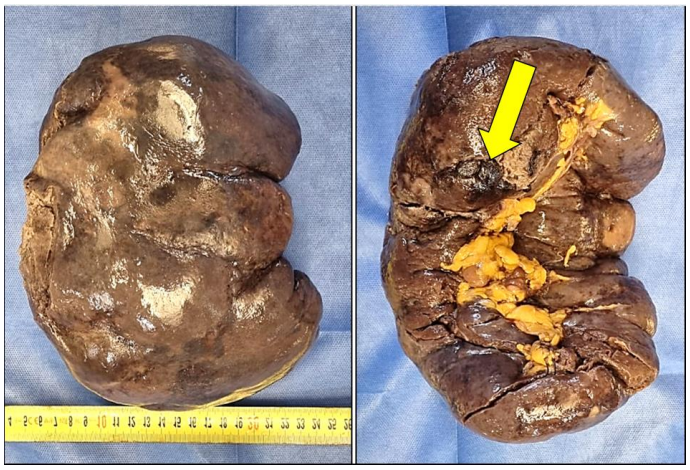

**Figure 2.** Spleen, macroscopic view. The yellow arrow highlights the subcapsular hematoma in the splenic hilum.

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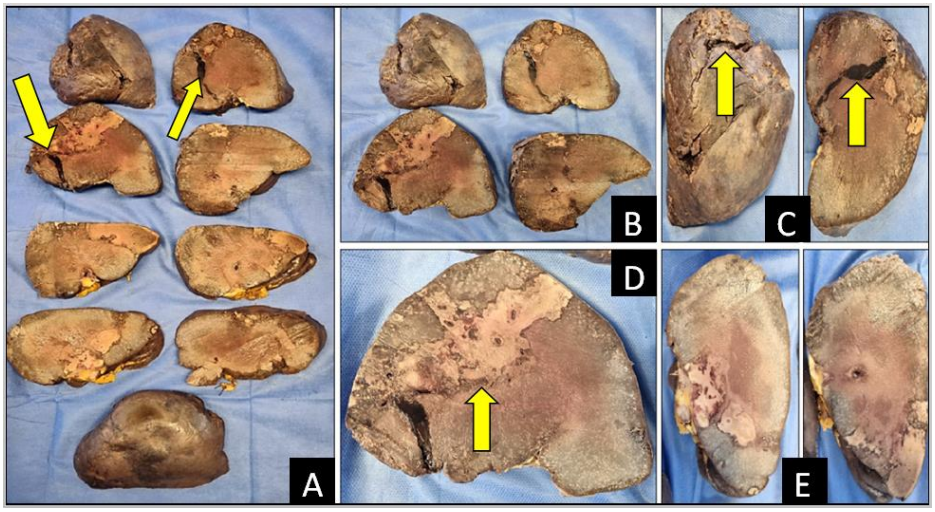


**Figure 3.** Transverse sections of the spleen. Yellow arrows showing areas of infarction (a-d), hemorrhage and hemorrhagic dissection (a-c).

*2.2. Histological and Immunohistochemical Findings*

Microscopic examination of the spleen with hematoxylin-eosin staining showed that the splenic tissue had a subverted structure caused by hemorrhagic phenomena, which partially dissected the parenchyma up to the perisplenium (Figure 5) in a serpiginous manner. This was associated with an abundance of abnormal tumor cells, particularly a monomorphic lymphoid proliferation of small—to medium-sized cells with irregular nuclear outlines (Figures 4 and 5).

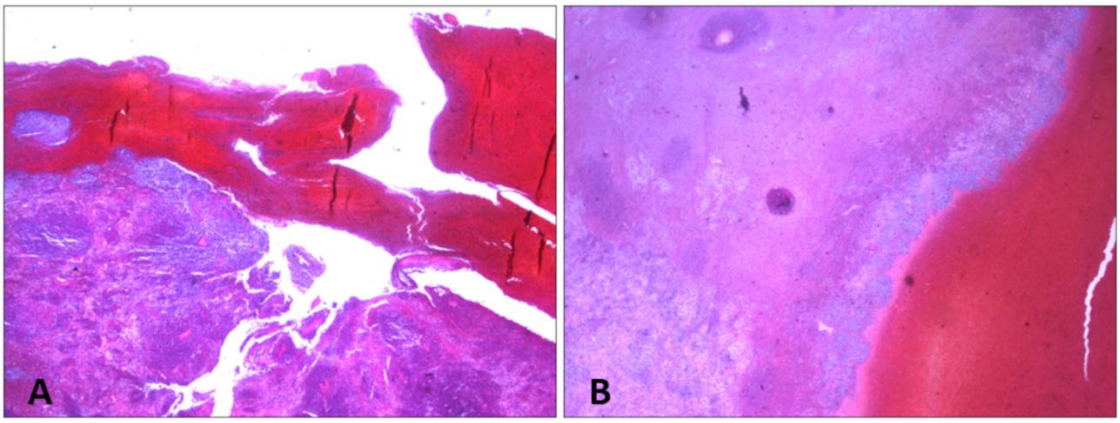


**Figure 4.** H&E staining of spleen samples. a) Sub-capsular hematoma is stratified under the capsule which appears fissured (10x); b) macrophages containing hemosiderin at the interface between hematoma and parenchyma (10x).

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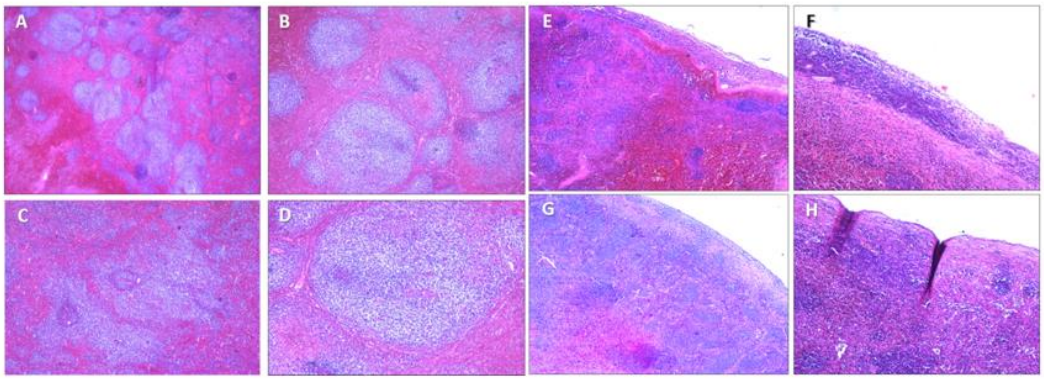


**Figure 5.** H&E staining of spleen samples. a-c) Numerous neoplastic follicles next to each other (back to back)(10x); d) Neoplastic follicle showing lack of polarization with random distribution of centrocytes and centroblasts, loss of a defined mantle area and absence of macrophages with dyeable body (10x); e-h) Perisplenium infiltrating mantle cell lymphoma with subcapsular hemorrhages (10x).

The time estimation of the subcapsular hematoma and hemorrhage was carried out with H&E, Van Gieson staining, and CD68 expression. The van Gieson staining highlighted perivascular fibrosis (Figure 6). Immunohistochemical analysis for CD68 revealed the presence of CD68-positive cells (Figure 7), namely histiocytic macrophages.

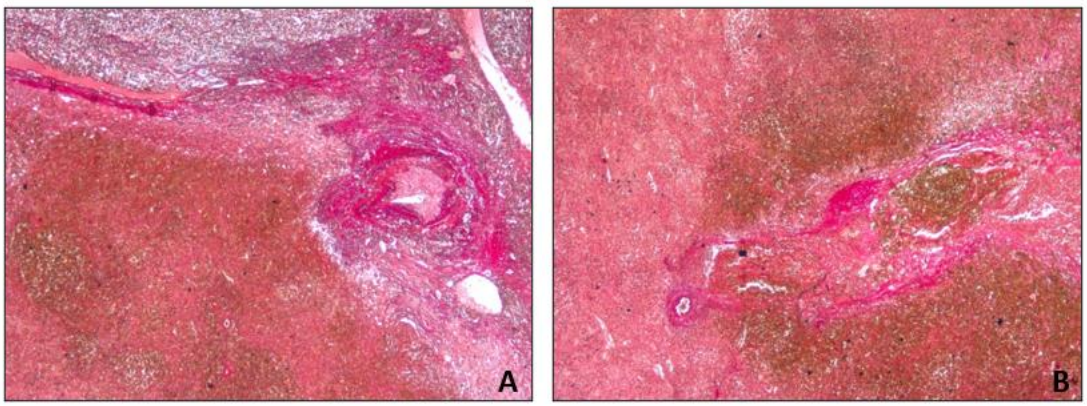


**Figure 6.** Spleen sections with Van Gieson staining. Perivascular fibrosis and hemorrhage ((a) 10x; (b) 20x). .

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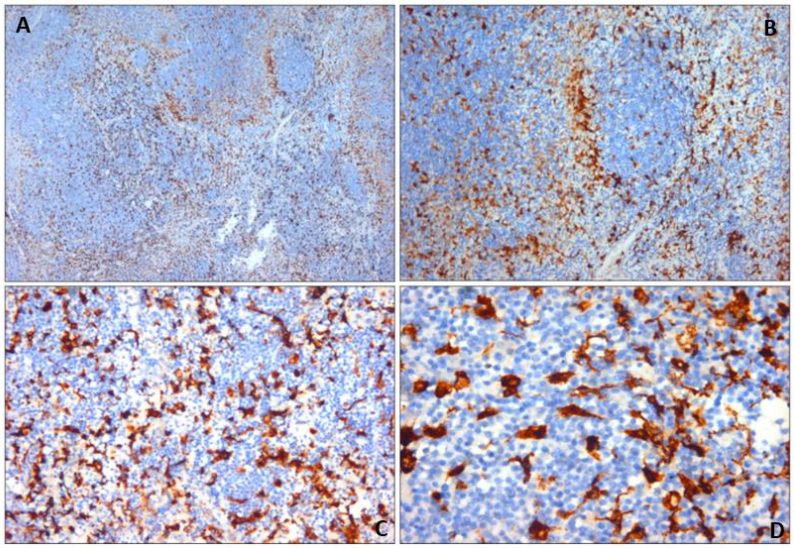


**Figure 7.** Spleen sections with CD68 immunohistochemical markers. Active histiocytes proliferation in splenic hematoma (a) 10x; b) 20x; c) 40x; d) 80x).

For the characterization of the spleen neoplasm, we used immunohistochemical investigations. Immunohistochemistry showed the presence of CD20, CD5 and BCl-2 positive cells (Figure 8).

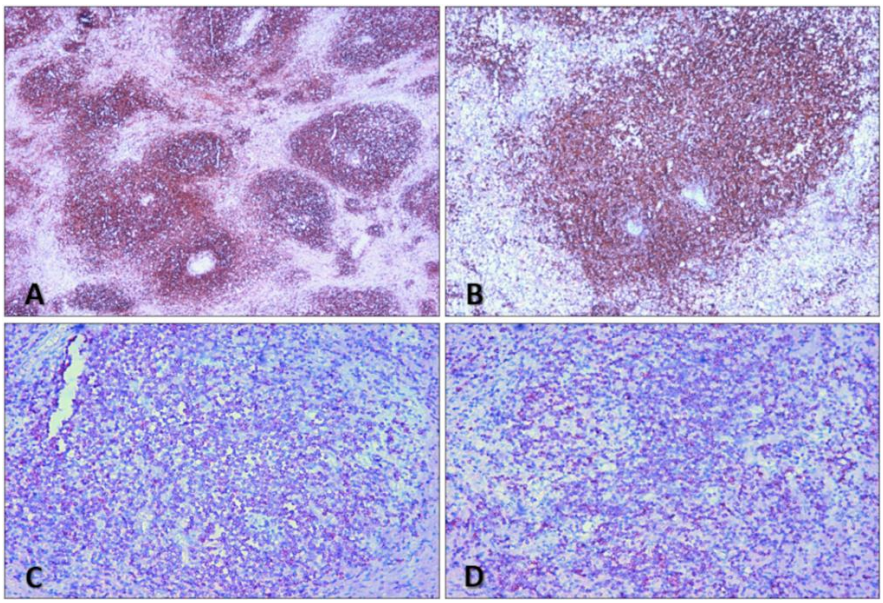


**Figure 8.** Spleen sections. a-b) CD20 expression (a 10x, b 20x). c-d) Bcl-2 expression (c,d 40X). Mantle cell lymphoma features.

Microscopic examination of the mesenteric and paratracheal lymph nodes was also performed. Lymph nodes were the site of widespread lymphomatous cell infiltration with the same monomorphic lymphoid proliferation of the spleen (Figure 16). Immunohistochemical analyses showed that lymphoid cells were BCl-2 +, CD5 +, and CD20 +, with a proliferation index (Ki67) of approximately 75% (Figure 9).

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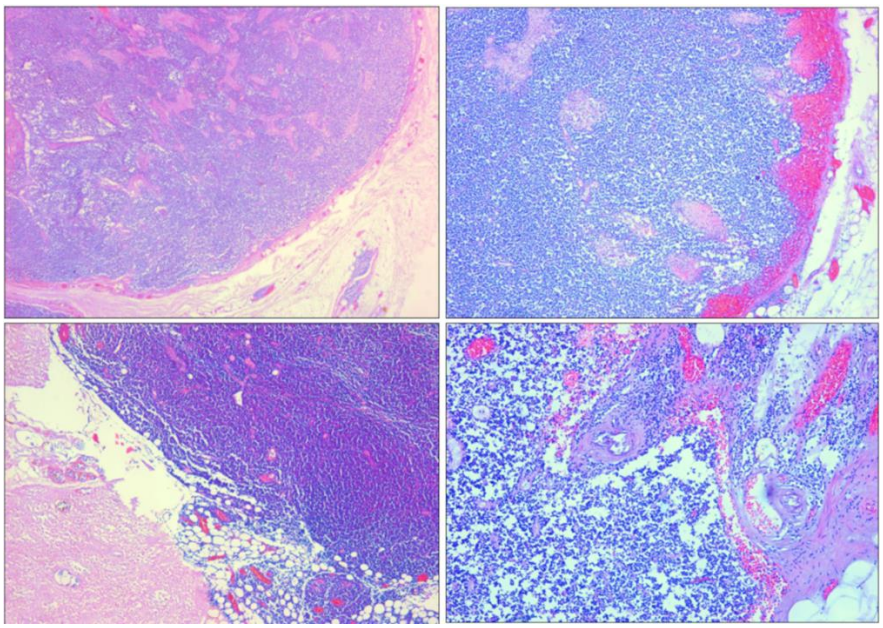

**Figure 9.** H&E staining Lymph Node section. Lymph node site of widespread lymphomatous cells infiltration.

Microscopic examination of bone marrow with haematoxylin-eosin staining and CD20 showed paratrabecular and intramedullary nodular lymphoid infiltration.

## 3. Discussion

Mantle cell lymphoma is a rare type of B cell non-Hodgkin lymphoma, representing less than 10% of NHLs. It usually occurs in the fifth decade and shows a predominance in the male sex. Mantle cell lymphoma is characterized by t (11;14) with CCND1-IGH fusion leading to overexpression of cyclin D1 (Bcl-1), a protein required for progression through the G1 phase of the cell cycle. It manifests with a spectrum of diseases ranging from relatively indolent to aggressive. High levels of cyclin D1 characterize immunophenotype. Most tumors also express CD19 and CD20. The tumor is generally CD5-positive and CD23-negative, which are useful characteristics to distinguish it from CLL/SLL (chronic lymphocytic leukemia/small lymphocytic lymphoma) [12].Tumor cells may surround the reactive germinal centers of the lymph node, resulting in a nodular appearance at low magnification, or they may subvert the typical architecture of the lymph node diffusely. Typically, the proliferation consists of a homogeneous population of small lymphocytes with irregular outlines. Chromatin is often condensed, nucleoli are inconspicuous, and cytoplasm is sparse. Sometimes, neoplasms of intermediate-sized cells with more dispersed chromatin and a high mitotic index are observed. At the time of diagnosis, most patients show generalized lymphadenopathy. Frequent extra lymph node involvement sites include bone marrow, spleen, liver, and gastrointestinal tract. Based on immunohistochemical analyses, the patient was diagnosed with mantle cell non-Hodgkin lymphoma, as evidenced by CD20, CD5, Bcl-2, and Ki-67 (>75%) positive cells. According to the Ann Harbor classification, the evidence of splenic, medullary, supra - and subdiaphragmatic lymph node involvement shows that the neoplasm was stage IV A.

The van Gieson staining and CD68 were particularly useful in highlighting the timing of subcapsular hematoma and necrotic infarction of the parenchyma [11]. The presence of perivascular fibrosis and histiocytic macrophages highlights how the repair process had already developed. Therefore, the splenic hematoma was compatible with a previous trauma and then with a two-stage rupture. Moreover, the timing of the rupture was consistent with a delayed splenic rupture due to the traumatic fall (within ten days approximately). The findings strongly suggest that the splenic rupture experienced after trauma may be associated with the patient's pre-existing hematological malignancy of the spleen. The cause of death was attributed to cardiocirculatory arrest due to

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hypovolemic shock in a patient subjected to splenectomy surgery for splenic rupture and severe hemoperitoneum due to an in-hospital fall, affected by mental-cell type B non-Hodgkin lymphoma (Stage IV A according to Ann-Arbor Staging System). The lymphoma diagnosis was performed after death through an autopsy. The lymphoproliferative disease was unknown previous autopsy.

This case highlights the importance of considering underlying hematological malignancies when investigating delayed traumatic splenic rupture. Histopathological and immunohistochemistry analyses are crucial in establishing accurate diagnoses in forensics, better understanding potential complications, guiding appropriate patient management. The study of erythrocytes, fibrinogen, platelets, and macrophages offers valuable insights into the progression of reparative processes linked to sub-capsular hematoma and the subsequent delayed splenic rupture. Our research underscores the significance of histochemical and immunohistochemical examination of sub-capsular splenic hematoma, yielding beneficial outcomes for determining the timeline of sub-capsular hematoma formation. However, establishing the causal connection between splenic rupture and a preceding traumatic event remains necessary [11]. Following the fall event, only a face and brain CT scan was performed in this case. In fact, in the hours following the fall, there were no signs or symptoms of abdominal involvement. It was not known that the patient had splenic lymphoma. Medical malpractice claims are encompassed within tort law, which addresses allegations arising from harm caused, typically grounded in the negligence tort. This legal framework hinges on principles such as duty of care, breach of duty, resulting damage, and establishing a causal link between the violation and the harm incurred [13]. Many falls that occur in the hospital are not preventable [14]. In Italy, according to Italian legislation clinical negligence may arise in case of lack of adherence highlights to evidence-based guidelines and good clinical practices in daily activity [15]. No lack of care, lack of surveillance, or lack of preventive actions emerged about the onset of falls. Criminal liability of physicians for the death was excluded, given the absence of signs and symptoms of abdominal involvement and the absence of clinical negligence and lack of surveillance from the medical records analysis. Patients with lymphoproliferative diseases with possible splenic localization should be subjected to more accurate clinical-instrumental monitoring in case of trauma since the risk of rupture exists and is known in the literature [7–10].

As outlined previously, spontaneous splenic rupture typically doesn't occur due to trauma. The individual was diagnosed with non-Hodgkin only after death and may have experienced a spontaneous splenic rupture. Considering the history of a fall and the timing (almost ten days) of the splenic rupture, according to the histological findings of splenic samples (presence of fibrin and macrophages in subcapsular hematoma), the rupture was considered more probably of traumatic origin, with an underlying pathology that contributed to it.

The rib cage typically protects the spleen against trauma. However, in cases of splenic pathology, the spleen becomes more susceptible to rupture due to changes in its consistency and because splenomegaly can cause the spleen to extend below the rib cage. Abdominal pain is typically the primary symptom of splenic rupture. The nature of this pain can vary, ranging from localized pain in the left upper quadrant to left-sided chest pain or generalized abdominal discomfort. Patients with splenic injuries may also experience symptoms such as nausea, vomiting, fainting, abdominal swelling, low blood pressure, rapid heartbeat, signs of peritoneal irritation, fever, anemia, and Kehr's sign (pain in the left shoulder due to irritation of the diaphragm). It's essential to consider the possibility of splenic injury in all patients with hematologic malignancies, even in the absence of trauma. The presentation of splenic injury in individuals with hematologic malignancies may differ from those with healthy spleens. Furthermore, in patients in whom the situation is unknown, it should be checked in the anamnesis that there are no symptoms suggestive of lymphoma since it may be a predisposing condition that exposes to a two-stage rupture, an event burdened by high mortality.

## 4. Conclusions

Hematological malignancies need to be considered as a contributing factor when investigating delayed traumatic splenic rupture. Histopathological and immunohistochemical analyses play a

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crucial role in diagnosing non-Hodgkin lymphoma and in assessing time estimation of splenic rupture. Van Gieson staining technique and immunohistochemical analysis with CD 68 marker are reliable methods to establish the time since trauma of subcapsular hematoma, an essential task in forensics when dealing with both violent deaths and medical malpractice issues. Patients with a history of lymphoproliferative disease should be subjected to more accurate clinical-instrumental monitoring in case of trauma since the existing risk of splenic rupture and mortality.

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**Institutional Review Board Statement:** Our investigations were carried out following the rules of the Declaration of Helsinki of 1975, revised in 2013. According to Italian legislation, ethical approval for a single case is not required, as long as the data are kept anonymous and the investigations performed do not imply genetic results.

**Informed Consent Statement:** The current Italian legislation requires neither the family's consent nor ethical approval for a single case, as long as the data are strictly kept anonymous. Because summoning the parents was not possible, as it would badly interfere with the grieving process, the parents' consent was completely waived, according to the Italian Authority of Privacy and Data Protection ("Garante della Privacy": GDPR nr 679/2016; 9/2016 and recent law addition number 424/19 July 2018; http://www.garanteprivacy.it).

**Data Availability Statement:** The data presented in this study are available on request from the corresponding author.

**Conflicts of Interest:** The authors declare no conflict of interest as there's no financial/personal interest or belief that could affect their objectivity.

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